UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/812,502	03/20/2001	Marilyn Anne Anderson	9748BZ	7221

7590 10/21/2003

SCULLY, SCOTT, MURPHY & PRESSER
400 Garden City Plaza
Garden City, NY 11530

EXAMINER	
SAIDHA, TEKCHAND	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/812,502	ANDERSON ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 22 September 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires *six* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *see Advisory*.

3. ☒ Applicant's reply has overcome the following rejection(s): none.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☐ The a)☐ affidavit, b)☐ exhibit, or c)☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *36*.

   Claim(s) objected to: _____.

   Claim(s) rejected: *33-35,37 and 38*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

10.16.03

Advisory Action

1. Applicants' Amendment After Final filed 09.22.03 is Acknowledged. The amendment After Final, however, is **not entered** because it raises new issues that would require further consideration and/or search. SEQ ID Nos. 17 & 18, are new addition to the specification and claims 33-34 & 37, previously not disclosed, will have to be searched.

2. Applicant's arguments filed as per the amendment cited as per Paper No. 9 and in view of new claims 33-38 currently pending have been fully considered but they are not deemed to be persuasive. The reasons are discussed following the rejection(s).

3. **Art Rejection:**

The arguments are not deemed persuasive over those already presented, which claims were and are rejected over the prior art of record.

112 Rejection :

The arguments are not deemed persuasive over those already presented, which claims were and are rejected, for the reasons of record.

4. Rejections (& arguments) made in the prior Office Action (Final) are repeated for Applicants' convenience.

5. ***Written Description***

Claims 33-35 & 37-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 33-35 & 37-38 are directed to any protease sensitive peptide or a nucleic acid encoding such a peptide 'the claimed genus', wherein X_1 & X_2 may be the same or different amino acid residues but preferably 'Lys' residues; and wherein R_1 & R_2 may be any of the amino acid residue or a peptide. The specification on page 10, lines 1-3 assumes that such a discovery of a protease sensitive peptide will enable the engineering of peptides and polypeptides capable of being processed in a plant by cleavage. No specific examples are presented, however. The prior art is silent about such or similar constructs that a skilled artisan could use in order to practice such an invention. The specification does not describe in clear terms even a single or representative number of species to the genus. A 'representative number of species' requires that the species which are expressly described be representative of the entire genus. Therefore, without a clear description of even a single functional protease sensitive peptide construct or the nucleic acid encoding the same, further modification that are expected to be made in substituting the R_1 & R_2 or X_1 & X_2 for other compounds would require adequate written description of the genus, which cannot be achieved by disclosing a generalized genus. In an unpredictable art, such as the instant one, wherein a peptide construct and the nucleic acid encoding such a construct - be made by amino acid or peptide group substitution, adequate written description requirement of a genus cannot be achieved by disclosing a generic formula without clear-cut identifying characteristics, such as structure or functional activity of the peptide construct or nucleic acid encoding the same, written description for each member within the genus will be necessary and such is not described. Therefore, the written description requirement is not satisfied.

Applicants arguments :

Applicants argue that the specification describes the general structure : R1-X1-X2-Asn-Asp-R2. The specification further provides an example of such a protease sensitive peptide of SEQ ID NO : 3 (protease inhibitor (PI) precursor) which is cleaved at six sites to produce seven peptides.

In response Applicants' SEQ ID NO : 3 is a 368 amino acid sequence which having cleavable sites is cleaved at six sites to produce seven peptides. Therefore, SEQ ID NO : 3 is the protease sensitive peptide and not the seven peptides. The seven peptides being the product of the cleavage.

6. ***Claim Rejections - 35 U.S.C. § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 33-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Williams [U.S.P. 5,032,396, July 16, 1991]. Williams teaches a peptide sequence (see Table 2) comprising the amino acid sequence : .....GLN-**LYS-LYS-ASN-ASP**-ALA..... [where X_1 & X_2 are Lys residues and R_1 are amino acid(s) GLN or residues 1-102 ; & R_2 are amino acid(s) ALA or residues 107-129] which by virtue of the structure is functionally a protease sensitive peptide, because protease acts between residues Asn-Asp. The claims are written so broadly as to be anticipated by the reference.

7. ***New Rejection***

Claims 33-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Sigma Peptides : Product Nos : T-5028 or T-5153 [Nature 321, 441 (1986)] or A-7907 [PNAS, USA., 79, 1443 (1982)].

T 5028 - TYR- ALA-GLY-ALA-VAL- **ASN- ASP** -LEU

T-5153 - TYR- GLY-ALA-VAL-VAL- **ASN- ASP** -LEU

A-7907 - ARG-ARG-LEU-ILE-GLU- **ASP-ASN** -GLU-TYR-THR-ALA-ARG-GLY

These peptides when read in the light of the claim limitations read upon the claims. As recites in claims 33-34, X1 and X2 can be the same or different amino acid residues - which may be more than one amino acid at each of the positions, which is clearly the same at the Sigma peptides, and being the same inherently qualify to be a protease-sensitive peptide. The other limitations of claims 33-34 are R2 which may be an amino acid or a peptide which is represented by the underlined amino acid LEU in Product Nos. T 5028 or T-5153; or the peptide -GLU-TYR-THR-ALA-ARG-GLY in Product Nos. A-7907, and is therefor anticipated.

8. ***Claim Rejections - 35 U.S.C. § 103***

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 37-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suggs et al. [Suggs et al.[PNAS, USA.,78(11) : 6613-6617] in view of Williams [U.S.P. 5,032,396, July 16, 1991].

Suggs et al. teach the use of mixtures of chemically synthesized oligodeoxyribonucleotides as hybridization probes for the isolation of specific cloned DNA sequences. The approach is to "chemically synthesize a mixture of oligonucleotides that represent all possible codon combinations for a small portion of the amino acid sequence of a given protein." Once a protein, in this case the protease of the generalized structure (R1- **X1- X2 -ASN-ASP**- R2) or the specific sequence [GLN-**LYS-LYS-ASN-ASP**-ALA] of Williams, is purified and known. Under the principle that one sequence must be complementary to the DNA for that protein, "the complementary oligonucleotide will form a perfectly base paired duplex with the DNA from the coding region...". Thus, mixed oligonucleotide probes allow the isolation of DNA sequences for any protein with a known or obtainable portion of the amino acid sequence.

In light of the method of Suggs et al. for isolating the appropriate DNA sequence coding for a particular protein, it would have been obvious to one of ordinary skill in the art to use these methods to determine the coding nucleotide sequence of protease in murine (IL-7) disclose the fact that murine produces the protease and therefore possesses that gene. The state of the art at the time the invention was made dictates that, since the culturing and recovery of the naturally-occurring enzyme from its natural source yields small, and at times unstable, amounts, production of such proteins by recombinant means is the single best technique to dramatically increase yield and insure stable production of the protein. One would not have to probe a library of possible sources to find a similar gene, as Williams provides sufficient motivation to merely determine the sequence from the known source. Thus, the nucleic acid molecule of the claim 23 is not considered patentable.

From this, one utilizing the ordinary level of skill in the art could easily assemble various expression vectors containing either a recovered full length clone, or the appropriate fragments ligated at the corresponding restriction sites. The transformation of host cells with this vector is also within the ordinary skill in the art, as a variety of cell lines, both prokaryotic and eukaryotic, human (mammalian) included, are well documented and commonly used. The selection of the appropriate plasmids, promoters, and cell lines for proper expression of the inserted gene is merely a matter of judicious selection, within the scope of ability of one ordinarily skilled in the art.

9. ***Double Patenting***

In view of Applicants filing of Terminal Disclaimer, the Double Patenting rejection previously made based upon U.S.P. 6,261,821, is withdrawn.

10. Applicants' further arguments do not relate to the claims as amended and filed as per the 'supplemental amendment', dated 3.28.03 (Paper No. 12) and is therefore not responded to.

11. Claim 36 is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (703) 305-6595. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group in the Technology Center is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Tekchand Saidha
Primary Examiner, Art Unit 1652
October 16, 2003